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Intractable Singultus: Atypical presentation of COVID 19

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ABSTRACT

Singultus are involuntary manoeuvre that involve the reflex arc of swallowing and can be further divided into acute singultus (<48 hours) or persistent singultus (>48hours). We present a case series of three patients of different age groups who presented with the chief complaint of persistent hiccup not responding to treatment. Other than Hiccup which was episodic physical examination of the patient were unremarkable. However, Reverese Transcriptase Polymerase Chain Reaction for COVID-19 was Positive and High-Resolution CT Scan of the Chest was able to demonstrate Ground Glass Opacities scattered throughout the lung. The patients did not respond to primary treatment for hiccups and were treated with antiviral and other supportive measures. All the three patients recovered and were later discharged in stable condition. Thus, this case series showcases the importance of keeping COVID-19 as an important differential diagnosis of persistent hiccup to be prompt in reaching the diagnosis in this atypical presentation but to also be vigilant of unexpected exposure for the physician himself.

Keywords: COVID-19, Singultus, Pneumonia

1. INTRODUCTION

Hiccups or Singultus are reflex movements which occur due to sudden and forced contraction of the intercostal and diaphragm muscle which is followed by abrupt closing of the epiglottis giving rise to the typical "hic" noise associated with hiccups. Hiccups can be classified as Acute (<48 hours) or Persistent (>48 hours). Majority of bouts of hiccups are transient and last less than 48 hours however persistent hiccups lasting further than two days of duration may be related to a serious underlying pathology and may also hamper the quality of life. Though, a specific cause for hiccups is not obtained always but a thorough history taking of the patient along with detailed physical examination and various diagnostic testing should be carried out to rule out various differential diagnosis and for drafting therapeutic strategies.

In the month of December 2019, A Novel Coronavirus which was known case COVID-19 was discovered in Wuhan, China. A case report 138 positive patients in Wuhan, China described fever, dry cough and fatigue as common presenting symptoms of COVID-19. Since then various case reports have been published identifying a broad range of presenting symptoms including but

not limiting to myalgia, headache, hemoptysis, anosmia and patients presenting with predominantly gastrointestinal symptoms (Bendersky & Baren, 1959).

We report a series of three cases across various age groups which presented with persistent hiccups as the only presenting symptom and later turned out to be positive for COVID 19.

2. CASE REPORT

First Case

A 49 year old Male presented to the outpatient department with the chief complaint of hiccups since 72 hours for which he was taking medications but had no symptom relief, Patient was a known case of Hypertension on regular medication however there was no history of diabetes mellitus or coronary artery disease and other chronic medical conditions. There was no history of cigarette smoking or malignancy in the past. There was no prior history of fever, sore throat, cough, nasal congestion, chest pain or breathlessness.

On General Physical Examination, patient was a febrile, pulse was 92 beats per minute, regular in rhythm and volume, Blood pressure was 132/88mm hg in right arm supine position, respiratory rate was 24 breaths per minute and oxygen saturation was 98% without oxygen supplementation. Systemic Examination including chest was unremarkable. An HRCT of Chest was carried out which showed multiple ill defined patchy ground glass opacities with consolidation and septal thickening in bilateral lung fields suggestive of viral pneumonia with a CT Severity Score of 10/25.and CORAD 5 (figure 1a).

Patient was admitted and started on injectable antibiotics in view of pneumonia along and laboratory investigations were done which are shown in Table 1. In view of HRCT findings Throat and nasal Swab were sent for Reverse Transcription Polymerase Chain Reaction (RTPCR) which turned out to be Positive for COVID-19. Patient was managed on Remdesavir, low molecular weight heparin, dexamethasone, Ivermectin and other supportive measures. Symptomatic Care was given and the patient was discharged following five days of admission in stable condition.

Second Case

A 22 Year Old Female reported to the emergency medicine department with the chief complaint of persistent hiccup since five days. She had no prior medical history of Hypertension, Diabetes Mellitus, Thyroid Disorder or Coronary Artery Disease. No prior history of Fever, Cough, Sore Throat or breathlessness was reported. Patient's Obstetric and Menstrual History was unremarkable. Patient denied cigarette smoking or malignancy. On General Physical Examination, patient was afebrile, pulse was 76 beats per minute, regular in rhythm and volume, Blood pressure was 110/74mm hg in right arm supine position, respiratory rate was 19 breaths per minute and oxygen saturation was 97% on rom air. Systemic Examination including Chest was unremarkable.

HRCT chest was done which showed multiple ill-defined patchy ground glass opacities with consolidation and septal thickening in bilateral lung fields suggestive of viral pneumonia with a CT Severity Score of 9/25 and CORAD 4 (figure 1b). Patient was admitted and was started on injectable antibiotics in view of pneumonia with injectable Metoclopramide 10mg TDS in view of persistent hiccups, however he did not respond well and had persistent hiccups. Laboratory Investigations are mentioned in table 1. Patient's Throat and Nasal Swab were sent for Testing of COVID-19 by Reverese Transcriptase Polymerase Chain Reaction (RTPCR) which came Positive. Patient was started on Remdesavir, Dexamethasone, low molecular weight heparin, Ivermectin and other supportive measures. Patient was discharged after three days as she was stable and is doing well on follow up.

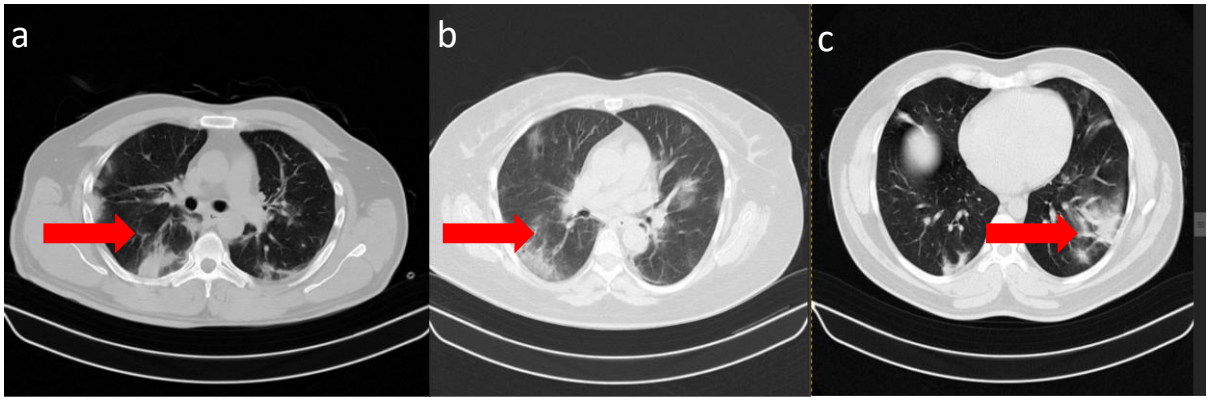
Third Case

A 70-year-old male Presented in the Out Patient Department with the Chief complaint of Persistent Hiccups since 8 days and loss of appetite. There was history of unintentional weight loss of 20 pounds over the span of five months. There was no history of Diabetes Mellitus, Hypetension or Coronary Artery Disease. There was no history of Fever, cough, sore throat or nasal congestion. Patient denied history of smoking and there was no history of malignancy in the past. There was no history of Parkinsonism or Anti Parkinson's drug intake. Patient gave history of intake of tablet baclofen since the past 3 days in view of persistent hiccups however there was only mild relief to his symptom.

On General Examination patient was afebrile, pulse was 84 beats per minute, regular in rhythm and volume, Blood pressure was 100/66mm hg in right arm supine position, respiratory rate was 24 breaths per minute and oxygen saturation was 95% on rom air. Systemic Examination including Chest was unremarkable. Patient's Throat and Nasal Swab for COVID-19 by Reverse Transcriptase Polymerase Chain Reaction (RTPCR) was sent and was found to be positive. HRCT Chest was done which revealed

multiple ill defined patchy ground glass opacities with consolidation and septal thickening in bilateral lung fields suggestive of viral pneumonia with a CT Severity Score of 12/25 and CORAD6 (figure 1c). Laboratory Investigations are shown in table 1.

Patient was admitted and started on injectable antibiotics, Remdesavir, Low Molecular Weight Heparin, Dexamethasone, Ivermectin, intermittent oxygen and other supportive measures. Patient Recovered following seven days of his treatment and was discharged.



HRCT of Case 1(a),Case 2 (b) and Case 3 [c] showing ground glass opacities involving the lower lobes suggestive of COVID19 infection

Figure 1 HRCT of case 1, 2 & 3

Table 1 Lab Investigations

Lab Paramteter	Case 1 AGE-49 Years SEX-MALE	Case 2 AGE-22 Years SEX-FEMALE	Case 3 AGE-70 Years SEX-MALE
CBC	Hb-12.3gm/dl MCV-86fl Platelet count-89000/dl WBC Count-4200/dl	Hb11.6gm/dl, MCV:82fl, Platelet count 1.16/dl, WBC Count 5200/dl	Hb-10.6gm/dl, MCV:79fl, Platelet count 760000/dl, WBC Count 4000/dl
LFT	Total Protein-6.4gm/dl, Albumin -3.0gm/dl, Globulin -3.4gm/dl, aspartate aminotransferase 26 units/l , alanine aminotransferase 28 units/l, Alkanline Phophatase 102 IU/l, Total Bilirubin :1.2mg/	Total Protein-7.0gm/dl, Albumin -3.6gm/dl, Globulin - 3.4gm/dl, aspartate aminotransferase 24 units/l , alanine aminotransferase 30 units/l, Alkanline Phophatase 98 IU/l, Total Bilirubin :0.9mg	Total Protein-6.1gm/dl, Albumin-2.9gm/dl, Globulin-3.2gm/dl, aspartate aminotransferase 33 units/l , alanine aminotransferase 28 units/l, Alkanline Phophatase 110 IU/l, Total Bilirubin :1.4mg/dl,
KFT	Creatinine:1.2mg/dl, Urea40mg/dl, Sodium131mmol/l, Potassium -4.8mmol/l	Creatinine:0.7mg/dl, Urea32mg/dl, Sodium34mmol/l, Potassium – 3.8 mmol/l	Creatinine:0.9mg/dl, Urea46mg/dl, Sodium-139 mmol/l, Potassium – 3.6 mmol/l
CRP	2.0mg/dl	1.7mg/dl	21.9mg/dl
D-Dimer	0.76	0.52	0.99
Serum Ferritin	200ng/ml	150ng/ml	750ng/ml
HRCT Score CORAD	10/25 5	9/25 4	12/25 6

3. DISCUSSION

Singultus is the medical term which is used for Hiccups which has it's origin from a Latin word singult which means a sob or gasp referring to the sound made by closing for glottis during a hiccup. Hiccups are sounds produced by forced contraction of diaphragm and intercostal muscles leading to closure of glottis (Newsholme, 1970). The exact physiology of a hiccup is complex and involves a reflex arc including the peripheral phrenic neve, vagus nerve and sympathetic pathway. The "Hiccup Centre" resides in the cervical spine and Brainstem which receive afferent fibers from Vagus and Phrenic nerve irritated by the bilateral lower lung infilteration in our case of lower lobe pneumonia due to COVID-19. It also receives afferent fibers from the sympathetic afferent fibers. The efferent fibers are sent through the Phrenic Nerve thus causing the contraction of diaphragm in Hiccup Reflex (figure 2).

Hiccups are a frequent phenomenon seen in humans and other animals including rats, cats and horses. They are reflex phenomenon that might expell air from the belly of a suckling infant frequently seen in mammals. More frequently seen in males, hiccups are usually benign and self-limiting and rarely require any medical intervention. Persistent hiccups are defined as hiccups more than 48 hours (Rousseau, 1995). Though looking like a innocent symptoms hiccups can point towards a serious underlying pathology. The Etiology of a hiccup can range from various causes starting from causes that are central such as a injury or a vascular disorder to various drugs like anti parkison and anti-psychotic drugs, Gastro oesphageal reflux disease, myocardial infaction, malignancies and dyselectrolytemia. Thus the work up of a patient with hiccup should be aimed to rule out the above etiologies. There is aenormous surge of information about clinical characteristics of Corona Virus Disease (COVID-19) which is an infectious disease which was crippled the world since it's emergence in 2019 through it's varied and unpredictable presentations and New data continues to be discovered throughout the world (Jain et al., 2021).

First described in Wuhan, China COVID-19 has led to widespread infection that has been a challenge for the phyisicans throughout the world to diagnose and treat (Wang et al., 2020). Pneumonia which is seen in COVID-19 patients is characteristically bilateral lower lobe predmoninant (Cui et al., 2019). Primary report of Pneumonia that presented as hiccup was reported in India by Dr Laha in 1951 where he reported a case of pneumonia in left lower lung presenting as hiccup. In such a patient involvement of the lower lobes of the lung leads to irritation of the diaphragm along with phrenic nerve and its pericardial branches causing hiccup.

Here, we present a case series of three cases presenting with persistent hiccups as the only presenting symptom in three different age groups with COVID-19 thus aiming at a keeping COVID-19 as an important differential of a person reporting with intractable hiccup. Our Patients were with antiviral medication in view of COVID-19 along with other supportive measures. All three of our patients recovered completely and were discharged and are doing well on follow up.

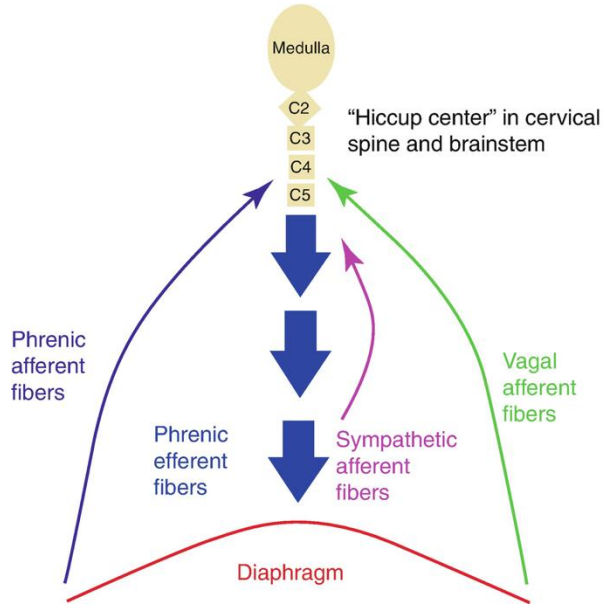


Figure 2 Showing the Hiccup Reflex Pathway

4. CONCLUSION

Important aspect highlighted by this case series is that Physicians should also keep COVID-19 as an important differential diagnosis in a patient reporting with the chief complaint of intractable hiccups to them as it an important atypical presentation of COVID-19. A vigilant mind with prompt investigations helps to uncover COVID-19 infection masquerading as an innocent hiccup which is a frequently encountered symptom in the outpatient department on day to day basis.

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Conflict of interest

The Authors have no conflicts of interest that are directly relevant to the content of this clinic-pathological case

Financial Resources

There are no financial resources to fund this study

Informed Consent

Informed Consent was obtained from the patient.

Author's Contribution

All the authors contributed equally to the case report.

Data and materials availability

All data associated with this study are present in the paper.

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